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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/785,158	02/23/2004	Martin C. Hinz	3364.25US-01	8497

24113 7590 07/09/2007

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EXAMINER	
KOLKER, DANIEL E	
ART UNIT	**PAPER NUMBER**
1649	

MAIL DATE	DELIVERY MODE
07/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/785,158	HINZ, MARTIN C.	
	Examiner	Art Unit	
	Daniel Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,16-18,21,28-32,46-50 and 54-62* is/are pending in the application.

4a) Of the above claim(s) *11,16-18,21,28-32 and 46-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *11,16-18,21,28-32,46-50,54-62* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks and amendments filed 23 April 2007 have been entered. Claims 1 – 10, 12 – 15, 19 – 20, 22 – 27, 33 – 45, and 51 – 53 are canceled; claims 54 – 62 are new. Claims 11, 16 – 18, 21, 28 – 32, 46 – 50, and 54 – 62 are pending.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 23 April 2007 has been entered.

Election/Restrictions

3. Claims 11, 16 – 18, 21, 28 – 32, and 46 – 50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2 May 2006.

4. Claims 54 – 62 are under examination.

5. The requirement for election of species with respect to specific dysfunctions (restriction requirement mailed 28 March 2006, page 3) is vacated. All claims currently under examination are generic with respect to disease. However the election of species with respect to specific neurotransmitter stands for the reasons of record.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 56 and 60 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 56 and 60 each recite the limitation "when a direct relationship is reached". The examiner is unable to find support this feature in the disclosure as originally-filed. The term "direct relationship" is not defined in the specification, and the originally-filed disclosure does not provide evidence of possession of this feature of the claimed invention, namely that a "direct relationship" between precursors administered and neurotransmitter levels is indicative of a "desired range".

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 56 and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 56 and 60 each recite the limitation "when a direct relationship is reached". It is unclear when this point would be reached, or how the skilled artisan could determine when it had been reached, or how the presence of a direct relationship is indicative of the neurotransmitter being in a "desired range". Figure 1 indicates several direct relationships. There is essentially no change in the Y-axis (serotonin level) from intervals 1 through 7 on the x-axis. That is, there is a direct relationship wherein every increase in X leads to no change in Y. There is also a direct relationship between X and Y from intervals 8 – 10, wherein every increase in X leads to a sharp increase in Y. As the term "direct relationship" is not defined in the specification, and there are multiple contradictory examples of such relationships between administration and neurotransmitter levels in Figure 1 of the disclosure, it is impossible to determine when the "neurotransmitter levels for the subject are in a desired range".

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 54 – 57 and 59 – 61 are rejected under 35 U.S.C. 102(b) as being anticipated by Ross (1999. The Diet Cure, of record).

Ross teaches methods of administering amino acid precursors of neurotransmitters to patients. A list of precursors is provided at p. 120 – 121 and includes 5-HTP, tyrosine, and phenylalanine, which are encompassed by independent claims 54 and 59 and recited in dependent claims 57 and 61. Ross also teaches that GABA, which is an amino acid neurotransmitter and needs no separate precursor, can be used; thus GABA is clearly both a "neurotransmitter" and an "amino acid neurotransmitter precursor" as recited in claims 54 and 59. At p. 128 – 129, Ross teaches the specific steps of the methods recited in claims 54 and 59. Ross teaches that the neurotransmitter precursors, also referred to as "aminos" or "amino acid therapy" are to be taken daily. Ross teaches that amino acid levels should be tested before therapy starts (which is on point to claims 54 – 55 and claim 59 part (a)) and again three month after therapy is ongoing (which is on point to claim 54 part (b) and claim 59 part (c). See paragraph spanning p. 128 – 129 and p. 129, item number 5 under "Action Steps". Note that the therapy is clearly to be administered multiple times per day (see pp. 127 – 128), so the test at the three-month point is quite clearly after administration of a first therapeutic amount of the amino acids. The administration of amino acid precursors is to continue for an additional three to twelve months (see Action Steps, number 6); thus the subsequent administration of amino acids is reasonably "a second therapeutic amount of neurotransmitter levels", which are administered to "the patient based on the assayed neurotransmitter levels of the subject". Note the final element of claims 54 and 59 (parts (d) and (e) respectively) requires that the testing and administration steps be repeated "until the neurotransmitter levels of the patient are in a desired range". No actual ranges are recited in the claims, and this element of the claims allows for no additional testing if the neurotransmitter levels are in fact already in the desired range. At p. 129 ("Tapering off Aminos") Ross clearly teaches when to stop administration of the amino acid precursors. Thus Ross teaches every element of independent claims 54 and 59.

Claim 55 is rejected as the reference by Ross teaches "an initial step of assaying" prior to administration of the amino acids (p. 129, bottom, step 5). Claims 56 and 60 are rejected as they depend from rejected base claims but recite no additional method steps. Absent evidence to the contrary, and particularly in light of the confusing nature of the phrase "a direct

relationship", it is reasonable that "a direct relationship" between the amount of amino acid precursors and corresponding neurotransmitter levels is achieved. Note particularly that Ross teaches that the amino acid supplements "will be needed only temporarily" (p. 129, middle of the page), implying that the requisite relationship is achieved. Claims 57 and 61 are rejected as several of the relevant neurotransmitters are explicitly described on pp. 120 – 121.

On p. 9 of the remarks filed 23 April 2007, applicant states "that new claims 54 – 62 are not anticipated by Ross." For the reasons set forth above, the prior art reference anticipates claims 54 – 57 and 59 – 61.

9. Claims 54 – 57 and 59 – 61 are rejected under 35 U.S.C. 102(b) as being anticipated by Siirtola (1975. Clin Neurol Neurosurg 78(2):77 – 88).

Siirtola teaches methods comprising measurement of the neurotransmitter dopamine in subjects' urine samples and administration of the dopamine amino acid precursor L-dopa (also called levodopa). Specifically, Siirtola teaches taking a first sample of a bodily fluid (urine) prior to the beginning of treatment (see p. 78, paragraph entitled "Levodopa treatment" for method and p. 80 first paragraph of Results for data). This is on point to claims 54, 55, and 59 step (a). Siirtola teaches administering a first therapeutic amount of amino acid precursors (levodopa) to the patients (see p. 78, paragraph entitled Levodopa treatment), which is on point to claim 54 step (a) and 59 step (b). Siirtola also teaches assaying a body fluid, particularly urine, after levodopa treatment had started. The collection of samples is described at p. 79, second complete paragraph. The neurotransmitter dopamine was assayed (p. 79 third complete paragraph). This step corresponds to claim 54 step (b) and claim 59 step (c). Siirtola teaches additional administration of L-dopa following the assays, which corresponds to claim 54 step (c) and claim 59 step (d). See p. 78 last complete paragraph which indicates the levodopa was administered throughout the protocol and urinary measurements were made after one, three, and six months, as well as p. 79 second paragraph which indicates that urine was collected over three successive days. As Siirtola teaches the repeated measurement of dopamine in the urine and continued administration of the neurotransmitter precursor levodopa for the duration of the protocol, the reference fairly teaches the "repeating" element set forth in claim 54 part (d) and claim 59 part (e). Thus Siirtola anticipates every element of claims 54, 55, and 59.

Claims 56 and 60 are rejected as the reference teaches that a direct relationship is achieved between levodopa administration and increase in excretion of dopamine (see p. 81

first complete paragraph which teaches that "treatment with levodopa induced a very highly significant ($P < 0.001$) in the excretion of DA [dopamine]."). Claims 57 and 61 are rejected as the neurotransmitter precursor L-dopa, also known as levodopa, was used.

10. Claims 54 and 56 – 57 are rejected under 35 U.S.C. 102(b) as being anticipated by 1A Technology 2(10); 15 October 2001.

1A Technology's newsletter teaches the method of claim 54. Specifically, at p. 1 column 2 – p. 2 column 1, the reference teaches administration of 5-HTP, which is an amino acid precursor of the neurotransmitter serotonin. Note step 4 teaches "start increase to 6 50mg 5-HTP 2 to 3 hours before bed **AND get a norepinephrine and serotonin urine test 5 days after the increase**." (emphasis in original). This clearly corresponds to claim 54, steps (a) and (b), which encompass administering a neurotransmitter precursor and assaying a bodily fluid to determine the amount of neurotransmitter levels. 1A Technology's newsletter also teaches that the urinary serotonin level should be between 1200 – 2400 (no units indicated in the reference) for appetite suppression (top of p. 2), and teaches that if the level is near the low end of that range "you may give 3 or 4 more 5-HTP and push the patient up to the top end of the range." This clearly corresponds to claim 54, part (c), "administering a second therapeutic amount of neurotransmitter precursors based on the assayed neurotransmitter levels of the subject". 1A Technology also teaches repeating the test as necessary (end of first paragraph of p. 2). Thus the prior art reference anticipates every step of claim 54. Claim 56 is rejected as it depends from rejected base claims but recite no additional method steps. Absent evidence to the contrary, and particularly in light of the confusing nature of the phrase "a direct relationship", it is reasonable that "a direct relationship" between the amount of amino acid precursors and corresponding neurotransmitter levels is achieved. Claim 57 is rejected as the reference specifically teaches administration of 5-HTP.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 54 – 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Siirtola (1975. Clin Neurol Neurosurg 78(2):77 – 88) in view of Ross (1999. The Diet Cure, of record).

The reasons why Siirtola anticipates claims 54 – 57 and 59 – 61 are set forth in the rejection under 35 USC § 103 above. Siirtola also teaches that 5-HIAA, which is the main metabolite of serotonin (5-HT), is reduced in the urine of Parkinsonian patients who are taking levodopa (see for example p. 81 second complete paragraph and p. 85 second complete paragraph). Siirtola also teaches that levodopa "displaces 5-HT from its storage sites... and both levodopa and DA exert an inhibitory influence on tryptophane hydroxylase, which governs the rate-limiting step in synthesis of 5-HT" (p. 85 second complete paragraph). However Siirtola does not teach administration of the neurotransmitter precursor 5-HTP as recited in claims 58 and 62.

Ross teaches that when serotonin (5-HT) levels are low, one effective way to boost serotonin levels is to consume 5-HTP. Specifically, at p. 123 second paragraph Ross teaches the artisan of ordinary skill "... another supplement you can take to boost serotonin is 5-HTP". Ross also discusses other amino acid precursors which could be used to increase dopamine levels (see p. 120), however Ross does not explicitly teach administration of L-dopa as recited in claims 58 and 62.

It would have been obvious to one of ordinary skill in the art to modify the method of Siirtola to administer both L-dopa and 5-HTP, with a reasonable expectation of success. The motivation to do so comes directly from the prior art references. Siirtola teaches assaying both dopamine and 5-HIAA, which are indicative of levels of dopamine and serotonin respectively, and teaches that administration of L-dopa increases dopamine but decreases the amount of serotonin. This provides the motivation to the skilled artisan to look for ways to boost serotonin, to compensate for this side effect of L-dopa administration. The reference by Ross directs the artisan of ordinary skill to administer 5-HTP to boost serotonin levels, thereby guiding selection of both L-dopa and 5-HTP as the neurotransmitter precursors to be administered, and arriving at the invention set forth in claims 58 and 62.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent

possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 54 – 62 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 – 29 of copending Application No. 11/282965. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in the '965 case would anticipate the claims in the instant case. The claims in the '965 case set forth additional steps beyond those explicitly recited in instant claims 54 – 62; however use of the open claim language "comprising" is inclusive of features and limitations beyond those recited in the claims. Thus the claims in the '965 case would anticipate the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Daniel E. Kolker
Patent Examiner

Daniel E. Kolker, Ph.D.
June 28, 2007